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EXAMINER
CHERESKIN, D

ART UNIT
1804

PAPER NUMBER
18

DATE MAILED: 06/10/92

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

☒ This application has been examined ☒ Responsive to communication filed on April 14, 1992 ☐ This action is made final.

A shortened statutory period for response to this action is set to expire three (3) month(s), _____ days from the date of this letter.
Failure to respond within the period for response will cause the application to become abandoned. 35 U.S.C. 133

Part I THE FOLLOWING ATTACHMENT(S) ARE PART OF THIS ACTION:

- | | |
|--|---|
| 1. <input checked="" type="checkbox"/> Notice of References Cited by Examiner, PTO-892. <u>3pp</u> | 2. <input checked="" type="checkbox"/> Notice re Patent Drawing, PTO-948. |
| 3. <input checked="" type="checkbox"/> Notice of Art Cited by Applicant, PTO-1449. <u>1p</u> | 4. <input type="checkbox"/> Notice of Informal Patent Application, Form PTO-152 |
| 5. <input type="checkbox"/> Information on How to Effect Drawing Changes, PTO-1474. | 6. <input checked="" type="checkbox"/> <u>interview summary</u> |

Part II SUMMARY OF ACTION

1. ☒ Claims 15-46 are pending in the application.
Of the above, claims _____ are withdrawn from consideration.
2. ☒ Claims 1-14 have been cancelled.
3. ☐ Claims _____ are allowed.
4. ☒ Claims 15-46 are rejected.
5. ☐ Claims _____ are objected to.
6. ☐ Claims _____ are subject to restriction or election requirement.
7. ☒ This application has been filed with informal drawings under 37 C.F.R. 1.85 which are acceptable for examination purposes.
8. ☐ Formal drawings are required in response to this Office action.
9. ☐ The corrected or substitute drawings have been received on _____. Under 37 C.F.R. 1.84 these drawings are ☐ acceptable; ☐ not acceptable (see explanation or Notice re Patent Drawing, PTO-948).
10. ☐ The proposed additional or substitute sheet(s) of drawings, filed on _____, has (have) been ☐ approved by the examiner; ☐ disapproved by the examiner (see explanation).
11. ☐ The proposed drawing correction, filed _____, has been ☐ approved; ☐ disapproved (see explanation).
12. ☐ Acknowledgement is made of the claim for priority under U.S.C. 119. The certified copy has ☐ been received ☐ not been received
☐ been filed in parent application, serial no. _____; filed on _____.
13. ☐ Since this application appears to be in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.
14. ☐ Other

EXAMINER'S ACTION

Claims 15-46 remain. Claims 1-14 are cancelled.

The database will be corrected to indicate that this is a continuation of 07/260,574 and that the filing date of '354 is 9/26/83.

5 The text of those sections of Title 35 U.S. Code not included in this action can be found in a prior Office action.

Claims 15, and 44-46 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

10 In claim 15, it is not clear how the insects are controlled. That is, are the transformed plant cells ground up and sprayed on a field or are the plant cells regenerated to form a transgenic plant which is planted in the field, etc.

Likewise, in claims 44-45, there is no recitation of specific method steps. The only method step implied is planting a plant.

15 In claim 46, it is not clear if resistance to all of the groups recited or any one of them is intended.

20 Claims 15-25 remain and new claims 26-46 are rejected under 35 U.S.C. 112, first and second paragraphs, as the claimed invention is not described in such full, clear, concise and exact terms as to enable any person skilled in the art to make and use the same, and/or for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

25 As recited previously in 260,574, the claims recite "a Bacillus thuringiensis crystal protein" (Claim 15(a), for example). However, Applicants have enabled the claimed invention for only one B. thuringiensis crystal protein which sequence is shown in Figure 1. Not only do different varieties of B. thuringiensis have different insecticidal proteins with varying homology to each other, but the same variety of B. thuringiensis may have

several insecticidal proteins. For example, Thorne et al points out that the subspecies kurstaki crystal contains at least 3 proteins with insecticidal activity (page 801, column 2, top, marked section; see other marked sections as well on pages 801 and 808-809). See also, Hofte et al, especially Tables 1-5. Therefore, it is necessary for Applicants to specify the particular B. thuringiensis var. kurstaki crystal protein claimed.

Applicants argue that the specification teaches a variety of insecticidal protein genes (Remarks, pages 18-20). Although the specification does teach a number of insecticidal protein genes, the claims encompass insecticidal protein genes which are deemed to be so dissimilar to the genes exemplified, that application of the claimed method to control insects and insecticidal plant cells as claimed are not enabled for one skilled in the art without undue experimentation for the reasons set forth in the previous office action and repeated above. Re Applicants' comments on the Hofte et al reference (Remarks, page 19, paragraph 3), it is not suggested that Applicants incorporate the nomenclature of Hofte et al into the present claims. However, claims limited to recite characteristics of the insecticidal protein genes described in the present specification might overcome this rejection. Limitation to genes derived from DNA encoding a Bacillus thuringiensis insecticidal crystal protein of about 130 kD (support in specification, page 66, for example) with toxicity to Lepidopteran insects (support in specification, page 64, for example) is suggested.

The rejection under 35 U.S.C. 112 first paragraph on pages 2-4 of the previous office action is withdrawn for claims 15-22, and 24-25 in view of the Declaration of Guy A. Cardineau.

The rejection of claims 15-25 under 35 U.S.C. 112, first paragraph, as the disclosure is enabling only for claims limited a full length Bacillus thuringiensis crystal protein gene where the insecticide encoding fragment is the insecticide encoding fragment found in any of pH450, pH577, or pH578 and the plant or plant cell is either of tomato or tobacco, and the toxic

activity is directed against Manduca sexta is withdrawn in view of the Cardineau Declaration and in favor of the new grounds of rejection set forth below.

5 Claims 23 and 26-46 are rejected under 35 U.S.C. 112, first paragraph, as the disclosure is enabling only for claims limited to transformed plant cells comprising a gene which encodes a Bacillus thuringiensis crystal protein fragment which includes the first 607 amino acids from the N-terminus of the B.t. protein in accordance with the teachings of the present specification. See MPEP 706.03(n) and 706.03(z).

10 It is noted that the Declaration of Guy A. Cardineau et al describes Exhibits 7 and 8 which teach plants transformed with pH585 which is described in the present specification (07/713,624) at page 135, for example. This construct encoded the first 607 amino acids from the N-terminus of the B.t. protein (present specification, page 133). Thus, the
15 claims should be appropriately limited. The rejection is maintained for the present broadly recited claims as it is not predictable that shorter truncations would be operable.

 Given this unpredictability, the limited guidance presented in the specification, and the breadth of the claims, it is deemed that undue
20 experimentation would be required of one skilled in the art to practice the invention as so broadly claimed, and that the claims should be limited to transformed plant cells comprising a gene which encodes a Bacillus thuringiensis crystal protein fragment which includes the first 607 amino acids from the N-terminus of the B.t. protein as disclosed in the Examples of
25 the instant specification and the Declaration of Guy A. Cardineau.

 Furthermore, enablement for plant cells containing such truncated B.t. genes is given the 10/21/88 date as plant cells containing such constructs are not exemplified in the previous specifications. Exemplification is considered necessary for enablement in this case in view of the

unpredictability of this art at the time of the claimed invention. Gelvin is relied upon to evidence that the expression of a foreign gene in a plant cell was unpredictable at the time of the claimed invention.

5 Claims 15-16, 19, and 22-25 remain and new claims 26, 28-29, and 39-46 are rejected under 35 U.S.C. 112, first paragraph, as the disclosure is enabling only for claims limited to dicot cells. See MPEP 706.03(n) and 706.03(z). Applicant's arguments have been fully considered but they are not deemed to be persuasive.

10 The rejection is maintained. Exhibits A through C are not convincing as none of the references teach transformed monocot plants. It is believed that the Vasil reference supports the position that transformation of monocots was not routine at the time of the claimed invention. Applicants' arguments, which focus on regeneration, are not persuasive for claims drawn to transformed plants and plant cells.

15 Regarding Applicants' Example 14 (page 140, present specification) and Exhibit 12 (paragraph 22, Declaration of Dr. Cardineau), while these examples discuss transformation of maize protoplasts, transformed plants are not described. The record indicates that Applicants consider the "cells of the invention [to] include those within plants" (Remarks, page 12, top). The
20 present specification and/or Declaration is not enabling for transformed monocot plant cells within plants and it is maintained that transformed monocots could not have been achieved without undue experimentation by one skilled in the art at the time of the claimed invention as evidenced by Vasil.

25 Claims 15-46 are rejected under 35 U.S.C. 112, first paragraph, as the disclosure is enabling only for claims limited to Bacillus thuringiensis crystal protein genes with toxicity to Lepidopteran insects. See MPEP 706.03(n) and 706.03(z).

As pointed out previously in 260,574, a given B.t. toxin does not show toxicity against all insect species (See Hofte et al, Table 5; Vaeck et al, page 37, column 1, for example). Thus, the specification is not enabling for insects in general, since insects which would be encompassed by the claims as now
5 recited vary considerably and one skilled in the art cannot predict that the B.t. crystal proteins of the present specification would have insecticidal activity against any other class of insect.

Given this unpredictability, the limited guidance presented in the specification, and the breadth of the claims, it is deemed that undue
10 experimentation would be required of one skilled in the art to practice the invention as so broadly claimed, and that the claims should be limited to Bacillus thuringiensis crystal protein genes with toxicity to Lepidopteran insects as disclosed in the Examples of the instant specification.

Claim 23 remains and new claims 26-27, 29-31, 34, 41-46 are
15 rejected under 35 U.S.C. § 102 (b) as being anticipated by Fischhoff et al.

As recited previously, Fischhoff et al disclose plant and plants cells which were insecticidal due to expression of truncated forms of a B.t. toxin gene. It is noted that Applicants are not entitled to the filing date of the parent application with respect to claims to truncated versions of the B.t.
20 gene (see below).

Claim 23 remains new claims 26-27, 33, and 41-46 are rejected under 35 U.S.C. § 102 (b) as being anticipated by Vaeck et al.

Vaeck et al disclose plant and plants cells which were insecticidal due to expression of truncated forms of a B.t. toxin gene. Although Vaeck et al
25 actually uses B.t. sequences from a different strain than that used by Applicants, Applicants' claims are so broadly recited that they are anticipated by Vaeck et al. It is noted that Applicants are not entitled to the

filing date of the parent application with respect to claims to truncated versions of the B.t. gene (see below).

Claims 23 and 26-27, 29-33, and 41-46 are rejected under 35 U.S.C. § 102 (b) as being anticipated by De Greve et al (EP-A 193259, publication
5 date September 3, 1986).

De Greve et al disclose plant and plants cells (tobacco) which were insecticidal due to expression of truncated forms of a B.t. toxin gene. It is noted that the De Greve et al reference predates the parent application 06/848,733. Insecticidal, transformed plants and plant cells with truncated
10 genes are not enabled in the grandparent application 06/535,354.

With respect to the rejections set forth above, Applicants argue that the first application exemplifies truncated genes at pages 37-39. This argument is not persuasive as the specification of the first application only teaches expression in bacterial cells, not in plant cells. Furthermore, the
15 truncated construct described in the first application has not been shown to be operable in subsequent applications and/or communications.

Claims 15-21, 23-39, 41-46 are rejected under 35 U.S.C. 103 as being unpatentable over either of Vaeck et al or Fischhoff et al taken with Wong et al, Held et al, or Klier et al.

20 Vaeck et al and Fischhoff et al disclose plant and plants cells which were insecticidal due to expression of truncated forms of a B.t. toxin gene. Although Vaeck et al actually uses B.t. sequences from a different strain than that used by Applicants, Applicants' claims are so broadly recited that they are obvious over either of Vaeck et al or Fischhoff et al. Furthermore, use of
25 sequences from the same strain as disclosed by Applicants or other B.t. strains in place of the insecticidal genes employed by Vaeck et al or Fischhoff et al would be obvious in view of the availability of such sequences as taught by Wong et al or Held et al or Klier et al. It is noted that

Applicants are not entitled to the filing date of the parent application with respect to claims to truncated versions of the B.t. gene (see above).

Therefore, the Vaeck et al and Fischhoff et al references may properly be applied to claims to a truncated B.t. gene expressed in plants.

5 Consequently, the modification of the methods for producing insecticidal plants and plant cells taught by Vaeck et al and Fischhoff et al using other B.t. toxin genes was well within the ordinary skill in the art at the time the claimed invention was made as adequately demonstrated by the secondary references. One of ordinary skill would have had a reasonable
10 expectation of success in view of the availability of B.t. sequences as indicated by the references and the guidelines provided by either Fischhoff et al or Vaeck et al. Thus the claimed invention as a whole was clearly prima facie obvious over the references, in the absence of sufficient, clear, and convincing evidence to the contrary.

15 Claims 15-21, 23-39, 41-46 are rejected under 35 U.S.C. 103 as being unpatentable over De Greve et al (EP-A 193259) taken with Wong et al, Held et al, or Klier et al.

 De Greve et al disclose plant and plants cells which were insecticidal due to expression of truncated forms of a B.t. toxin gene. It is noted that the
20 De Greve et al reference predates the parent application 06/848,733. Insecticidal, transformed plants and plant cells and truncated genes are not enabled in the grandparent application 06/535,354. Therefore, application of the De Greve et al reference to the present claims is proper.

 While De Greve et al may not use exactly the same insecticidal gene
25 sequences as claimed by Applicants, use of sequences from the same strain as disclosed by Applicants or other B.t. strains in place of the insecticidal genes employed by De Greve et al would be obvious in view of the availability of such sequences as taught by Wong et al or Held et al or Klier et al.

Consequently, the modification of the methods for producing insecticidal plants and plant cells taught by De Greve et al using other B.t. toxin genes was well within the ordinary skill in the art at the time the claimed invention was made as adequately demonstrated by the secondary
5 references. One of ordinary skill would have had a reasonable expectation of success in view of the availability of B.t. sequences as indicated by the references and the guidelines provided by De Greve et al. Thus the claimed invention as a whole was clearly prima facie obvious over the references, in the absence of sufficient, clear, and convincing evidence to the contrary.

10 The rejection of claims 15-21 and 23-25 under 35 U.S.C. 103 as being unpatentable over Bevan et al, Fraley et al, Herrera-Estrella et al, or Barton et al. taken with Wong et al, Held et al, or Klier et al et al further in view of Brinster et al is withdrawn in view of Applicants' arguments.

15 Claims 22 and 40 are held free of the prior art in view of the operability of full length constructs in plant cells demonstrated by the Cardineau Declaration.

No claim is allowed.

The amendment to page 86, line 4 could not be entered. Applicants need to cancel the entire illustration and resubmit.

20 An inquiry concerning this communication should be directed to Che Swyden Chereskin, Ph.D., at telephone number (703) 308-1180. Inquiries of a general nature should be directed to the Group 180 secretary at (703) 308-0196.

25 Papers related to this application may be submitted to Group 180 by facsimile transmission. Papers should be faxed to Group 180 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform

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with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center number is (703) 308-4227.

**CHE S. CHERESKIN
PATENT EXAMINER
GROUP 180**

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*Che Surgen Chereskin
8/5/92*